

CLAIMS

What is claimed is:

1. A method for inducing the expression of at least one gene selected from group consisting of: AH CY, CCND2, ASS, FKBP52, PBEF, TRAP1, FABP52, G0S2,
5 PPIF, hsRBP8, fibrillarin, TFRC, CksHs2, SLC16A1, IARS, HLA-DRB1, GRPE-homolog, GPI, HSPD1, HDGF, SF2, coup transcription factor, RPS11, EIF5A and EIF4 γ in a mammalian cell comprising inducing MYC expression in said cell.
2. The method of Claim 1, wherein MYC expression is induced in the cell by
10 transfecting or transducing the cell with a recombinant fusion gene that expresses a chimeric receptor comprising MYC and a ligand binding domain and contacting the resulting cell with a corresponding ligand thereby inducing MYC expression.
3. The method of Claim 2, wherein the recombinant fusion gene directs the
15 expression of a fusion protein comprising MYC and the ligand binding domain of the estrogen receptor and wherein the ligand is 4-hydroxytamoxifen.
4. The method of Claim 2, wherein the ratio of the expression level observed in cells in the presence of ligand to the expression level observed in cells in the absence of ligand is greater than 2.
- 20 5. The method of Claim 2, wherein the cell is a primary human cell.
6. A method for repressing the expression of at least one gene selected from group consisting of: AH CY, CCND2, ASS, FKBP52, PBEF, TRAP1, FABP52, G0S2, PPIF, hsRBP8, fibrillarin, TFRC, CksHs2, SLC16A1, IARS, HLA-DRB1,

004032" 8662263

GRPE-homolog, GPI, HSPD1, HDGF, SF2, coup transcription factor, RPS11, EIF5A and EIF4 γ in a mammalian cell comprising inhibiting MYC expression in said cell.

- 09732998-120700
7. A method for causing transcriptional repression of at least one gene selected
5 from the group consisting of: A2M, TPM1, PDGFRA, FN1, CTGF, COL3A1, CDKN1A and a dithiolethione-inducible gene in a mammalian cell comprising inducing MYC expression.
 8. The method of Claim 7, wherein MYC expression is induced in the cell by
10 transfecting or transducing the cell with a recombinant fusion gene that expresses a chimeric receptor comprising MYC and a ligand binding domain and contacting the resulting cell with an appropriate ligand thereby inducing MYC expression.
 9. The method of Claim 8, wherein the recombinant fusion gene directs the
15 expression of a fusion protein comprising MYC and the ligand binding domain of the estrogen receptor and wherein the ligand is 4-hydroxytamoxifen.
 10. The method of Claim 8, wherein the ratio of the expression level observed in cells in the presence of ligand to the expression level observed in cells in the absence of ligand is less than 0.5.
 11. The method of Claim 7, wherein the cell is a primary human cell.
 - 20 12. A method for inducing at least one gene selected from the group consisting of: A2M, TPM1, PDGFRA, FN1, CTGF, COL3A1, CDKN1A and a dithiolethione-inducible gene in a mammalian cell comprising inhibiting MYC expression.

13. A method for identifying an agent that regulates MYC-dependent transcriptional regulation of gene expression comprising the steps of:
- a) obtaining an indicator cell that expresses a chimeric receptor comprising MYC and a ligand binding domain;
 - b) contacting the resulting indicator cell with an appropriate ligand in the presence and absence of an agent to be evaluated for its ability to regulate MYC's transcriptional regulation activity;
 - c) isolating mRNA from a plurality of indicator cells; and
 - d) comparing the level of gene expression in the indicator cells in the presence or absence of the agent
- such that if the effect of MYC on the expression of the gene is enhanced or inhibited in the presence and not the absence of the agent, then the agent regulates MYC-dependent transcriptional regulation of gene expression.
14. The method of Claim 13, wherein the agent is tested for its ability to inhibit MYC-dependent transcriptional regulation of gene expression.
15. The method of Claim 13, wherein the agent is tested for its ability to activate MYC-dependent transcriptional regulation of gene expression.
16. The method of Claim 13, wherein the gene whose level of expression is being evaluated for regulation is selected from the group consisting of: AHCY, CCND2, ASS, FKBP52, PBEF, TRAP1, FABP52, G0S2, PPIF, hsRPB8, fibrillarin, TFRC, CksHs2, SLC16A1, IARS, HLA-DRB1, GRPE-homolog, GPI, HSPD1, HDGF, SF2, coup transcription factor, RPS11, EIF5A and EIF4γ, A2M, TPM1, PDGFRA, FN1, CTGF, COL3A1, CDKN1A and a dithiolethione-inducible gene.

17. The method of Claim 13, wherein the chimeric receptor comprises MYC and the ligand binding domain of the estrogen receptor and wherein the ligand that induces *c-myc* is 4-hydroxytamoxifen.
18. The method of Claim 16, wherein the agent is evaluated in the presence of cycloheximide.
19. The method of Claim 13, wherein the level of gene expression is determined by hybridization to an oligonucleotide microarray.
20. The method of Claim 13, wherein the level of gene expression is determined by Northern blot analysis.
21. A method for treating cell proliferative disorders by altering the transcriptional regulatory activity of MYC in cells.
22. The method of Claim 21, wherein the cells are hematopoietic cells.
23. A method for treating cell proliferative disorders by altering MYC expression in cells.
24. The method of Claim 23, the cells are hematopoietic cells.
25. A method for detecting cell proliferative disorders comprising the steps of:
- a) isolating a cell of interest;
 - b) determining the level of expression of at least one gene that is regulated by MYC; and
 - c) comparing the level of expression in the cell of interest and cells that are not characterized as having a proliferative disorder of the gene in step b)

such that altered expression of the gene is indicative of a proliferative disorder.

26. The method of Claim 25, wherein the isolated cell is a hematopoietic cell.
27. The method of Claim 25, wherein the gene in step b) is selected from the group
5 consisting of: AHCY, CCND2, ASS, FKBP52, PBEF, TRAP1, FABP52, G0S2, PPIF, hsRPB8, fibrillarin, TFRC, CksHs2, SLC16A1, IARS, HLA-DRB1, GRPE-homolog, GPI, HSPD1, HDGF, SF2, coup transcription factor, RPS11, EIF5A and EIF4 γ , A2M, TPM1, PDGFRA, FN1, CTGF, COL3A1, CDKN1A and a dithiolethione-inducible gene.
- 10 28. A method for evaluating anti-proliferative drug candidates comprising the steps of:
- a) contacting a cell that conditionally expresses MYC with the anti-proliferative drug candidate;
 - b) inducing MYC expression;
 - 15 c) isolating mRNA from the cell; and
 - d) comparing the level of gene expression of at least one MYC-regulated gene in cells in the presence or absence of the anti-proliferative drug candidate
- wherein a difference in expression indicates the effect of the anti-proliferative drug
20 candidate on the transcriptional regulatory activity of MYC.
29. The method of Claim 28, wherein the anti-proliferative drug candidate is evaluated in hematopoietic cells.
30. A method for detecting MYC target genes comprising the steps of:
- a) inducing MYC expression in an indicator cell;

093298-12000

- b) isolating mRNA from induced indicator cells; and
 - c) comparing the level of gene expression of at least one mRNA transcript in cells induced for MYC expression with the level of gene expression of the mRNA transcript in cells that have not been induced for MYC
- 5 expression,

wherein altered expression of the gene corresponding to the mRNA transcript in MYC-induced cells indicates the gene is a MYC target gene.

31. The method of Claim 30, wherein the level of gene expression is determined using a hybridization assay.

10 32. The method of Claim 31, wherein the hybridization assay comprises a step of contacting cellular mRNA with an oligonucleotide microarray fused to a chip.

33. The method of Claim 32, wherein the chip is selected from the group consisting of: Affymetrix HUM6000-1, Affymetrix HUM6000-2, Affymetrix HUM6000-3 and Affymetrix HUM6000-4.

15 34. A method for inducing the expression of at least one gene selected from group consisting of: AHCY, CCND2, ASS, FKBP52, TRAP1, FABP52, G0S2, PPIF, fibrillarin, TFRC, CksHs2, SLC16A1, IARS, GRPE-homolog, HDGF, and EIF5A in a mammalian cell comprising inducing MYC expression in said cell.

20 35. A method for causing transcriptional repression of at least one gene selected from the group consisting of: A2M, TPM1, PDGFRA, FN1, CTGF, COL3A1, and CDKN1A in a mammalian cell comprising inducing MYC expression.

004027 866260